– *impurities C, E*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);
– *any other impurity*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);
– *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent);
– *disregard limit*: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

The thresholds indicated under Related substances (Table 2034.-1) in the general monograph *Substances for pharmaceutical use (2034)* do not apply.

Iron (*2.4.9*): maximum 5 ppm.

Dissolve the residue from the test for sulphated ash in *water R* and dilute to 10.0 ml with the same solvent.

Water (*2.5.12*): 10.4 per cent to 13.4 per cent, determined on 0.10 g.

Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 2.0 g.

ASSAY

Dissolve 0.500 g in 120 ml of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 ml of *0.1 M perchloric acid* is equivalent to 66.88 mg of $C_{34}H_{40}N_2O_{10}S$.

STORAGE

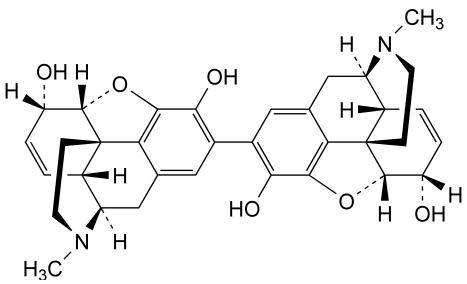
Protected from light.

IMPURITIES

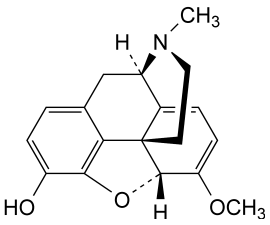
Specified impurities: *B, C, E.*

Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical use (2034)*. It is therefore not necessary to identify these impurities for demonstration of compliance. See also *5.10. Control of impurities in substances for pharmaceutical use*): *A, D, F.*

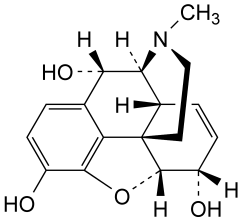
A. codeine,



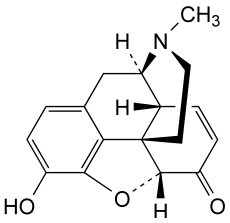
B. 7,7′,8,8′-tetradehydro-4,5α:4′,5′α-diepoxy-17,17′-dimethyl-2,2′-bimorphinanyl-3,3′,6α,6′α-tetrol (2,2′-bimorphine),



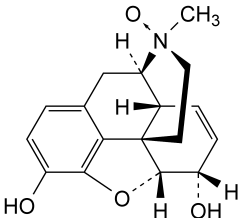
C. 6,7,8,14-tetradehydro-4,5α-epoxy-6-methoxy-17-methylmorphinan-3-ol (oripavine),



D. 7,8-didehydro-4,5α-epoxy-17-methylmorphinan-3,6α,10α-triol (10*S*-hydroxymorphine),



E. 7,8-didehydro-4,5α-epoxy-3-hydroxy-17-methylmorphinan-6-one (morphinone),

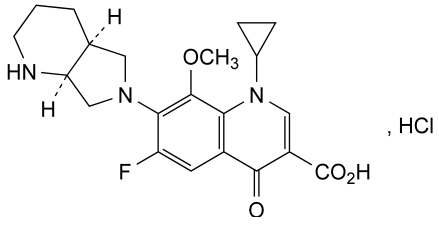


F. (17*S*)-7,8-didehydro-4,5α-epoxy-17-methylmorphinan-3,6α-diol 17-oxide (morphine *N*-oxide).

01/2008:2254
corrected 6.2

MOXIFLOXACIN HYDROCHLORIDE

Moxifloxacini hydrochloridum



$C_{21}H_{25}ClFN_3O_4$ M_r 437.9

DEFINITION

1-Cyclopropyl-6-fluoro-8-methoxy-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid hydrochloride.

Content: 98.0 per cent to 102.0 per cent (anhydrous substance).

PRODUCTION

The production method is validated to demonstrate the satisfactory enantiomeric purity of the final product.

CHARACTERS

Appearance: light yellow or yellow powder or crystals, slightly hygroscopic.

Solubility: sparingly soluble in water, slightly soluble in ethanol (96 per cent), practically insoluble in acetone.

IDENTIFICATION

A. Specific optical rotation (see Tests).

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *moxifloxacin hydrochloride CRS*.

C. Dissolve 50 mg in 5 ml of *water R*, add 1 ml of *dilute nitric acid R*, mix, allow to stand for 5 min and filter. The filtrate gives reaction (a) of chlorides (*2.3.1*).

TESTS

Appearance of solution. The solution is not more opalescent than reference suspension II (*2.2.1*) and not more intensely coloured than reference solution GY_2 (*2.2.2, Method II*). If intended for use in the manufacture of parenteral dosage forms, the solution is clear (*2.2.1*) and not more intensely coloured than reference solution GY_2 (*2.2.2, Method II*).

Dissolve 1.0 g in 20 ml of *dilute sodium hydroxide solution R*.

pH (*2.2.3*): 3.9 to 4.6.

Dissolve 0.10 g in 50 ml of *carbon dioxide-free water R*.

Specific optical rotation (*2.2.7*): – 125 to – 138 (anhydrous substance).

Dissolve 0.200 g in 20.0 ml of a mixture of equal volumes of *acetonitrile R* and *water R*.

Related substances. Liquid chromatography (*2.2.29*). *Carry out the test protected from light.*

Solution A. Dissolve 0.50 g of *tetrabutylammonium hydrogen sulphate R* and 1.0 g of *potassium dihydrogen phosphate R* in about 500 ml of *water R*. Add 2 ml of *phosphoric acid R* and 0.050 g of *anhydrous sodium sulphite R*, then dilute to 1000.0 ml with *water R*.

Test solution (a). Dissolve 50.0 mg of the substance to be examined in solution A and dilute to 50.0 ml with the same solution.

Test solution (b). Dilute 2.0 ml of test solution (a) to 20.0 ml with solution A.

Reference solution (a). Dissolve 50.0 mg of *moxifloxacin hydrochloride CRS* in solution A and dilute to 50.0 ml with the same solution. Dilute 2.0 ml of this solution to 20.0 ml with solution A.

Reference solution (b). Dissolve 5 mg of *moxifloxacin for peak identification CRS* (containing impurities A, B, C, D and E) in solution A and dilute to 5.0 ml with the same solution.

Reference solution (c). Dilute 1.0 ml of test solution (a) to 100.0 ml with solution A. Dilute 1.0 ml of this solution to 10.0 ml with solution A.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;

– *stationary phase*: *end-capped phenylsilyl silica gel for chromatography R* (5 µm);

– *temperature*: 45 °C.

Mobile phase: mix 28 volumes of *methanol R* and 72 volumes of a solution containing 0.5 g/l of *tetrabutylammonium hydrogen sulphate R*, 1.0 g/l of *potassium dihydrogen phosphate R* and 3.4 g/l of *phosphoric acid R*.

Flow rate: 1.3 ml/min.

Detection: spectrophotometer at 293 nm.

Injection: 10 µl of test solution (a) and reference solutions (b) and (c).

Run time: 2.5 times the retention time of moxifloxacin.

Identification of impurities: use the chromatogram supplied with *moxifloxacin for peak identification CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A, B, C, D and E.

Relative retention with reference to moxifloxacin (retention time = about 14 min): impurity A = about 1.1; impurity B = about 1.3; impurity C = about 1.4; impurity D = about 1.6; impurity E = about 1.7.

System suitability: reference solution (b):

– *resolution*: minimum 1.5 between the peaks due to moxifloxacin and impurity A;

– the chromatogram obtained is similar to the chromatogram supplied with *moxifloxacin for peak identification CRS*.

Limits:

– *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity B = 1.4; impurity E = 3.5;

– *impurities A, B, C, D, E*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1 per cent);

– *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.10 per cent);

– *total*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.3 per cent);

– *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.05 per cent).

Water (*2.5.12*): maximum 4.5 per cent, determined on 0.200 g.

Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g in a platinum crucible.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modification.

Injection: test solution (b) and reference solution (a).

Calculate the percentage content of $C_{21}H_{25}ClFN_3O_4$ from the declared content of *moxifloxacin hydrochloride CRS*.

STORAGE

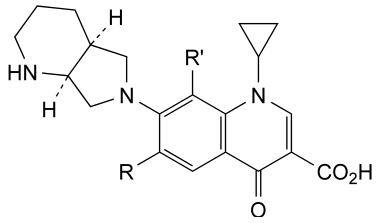
In an airtight container, protected from light.

LABELLING

The label states, where applicable, that the substance is suitable for use in the manufacture of parenteral dosage forms.

IMPURITIES

Specified impurities: A, B, C, D, E.



A. R = R′ = F: 1-cyclopropyl-6,8-difluoro-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,

B. R = R′ = OCH_3: 1-cyclopropyl-6,8-dimethoxy-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,

C. R = F, R′ = OC_2H_5: 1-cyclopropyl-8-ethoxy-6-fluoro-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,

D. R = OCH_3, R′ = F: 1-cyclopropyl-8-fluoro-6-methoxy-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,

E. R = F, R′ = OH: 1-cyclopropyl-6-fluoro-8-hydroxy-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid.